PURPURA HEMORRHAGICA WITH GENERALIZED INFECTION WITH *BACILLUS PARATYPHOSUS*.*

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Opinions are at variance as to the propriety of recognizing a new disease, "paratyphoid fever," in certain infections with *Bacillus paratyphosus*.[1] The chief reasons for doing so at present are the agglutinative properties of the blood serum and the results of bacteriologic investigations of the blood during life and of the body post-mortem. Skepticism concerning the value of agglutinative reactions of the blood serum as the only reliable means of recognizing the occurrence of such infections is found in the writings of Jürgens, Drigalski, Grünberg and Rolly, Conradi and Kayser, and others;[2] furthermore, since the anatomic entity established by Wells and Scott[3] considerable evidence has accumulated of the occurrence of *Bacillus paratyphosus* as an etiologic factor in food poisonings, Trautmann[4] especially maintaining that paratyphoid fever is a subacute meat poisoning.[5] It would seem best perhaps, for the present at least, to concede to the paratyphoid infections more of etiologic than of anatomic or clinical entity, pending the accumulation of an adequate number of carefully studied cases to permit of satisfactory nosologic classification. The case reported here offers some features of exceptional interest.

Clinical history.—The patient, a Canadian woman, 36 years of age, married 10 years, entered the Presbyterian Hospital on May 21, 1906, to the service of Dr. Bevan, to whom we are indebted for the opportunity to study and report the case. For over a month she had suffered from drowsiness, depression, and indisposition to work, and during this period experienced a regular evening rise of temperature which at times reached 103° F. Her appetite was poor, and for 10 days she was troubled with a dry cough. There was some tenderness over the abdomen, occasionally becoming localized in the left iliac region. The attending physician reported that two examinations of the blood serum had been made for its agglutinative action on typhoid bacilli,

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[1] Ascoli, *Zeitschr. f. klin. Med.*, 1903, 48, p. 418; Kolle, *ibid.*, 1906, 52, p. 285.

[2] See Boycott, *Jour. Hyg.*, 1906, 6, p. 33.

[3] *Jour. Infect. Dis.*, 1904, 1, p. 72.

[4] *Zeitschr. f. Hyg.*, 1904, 46, p. 68.

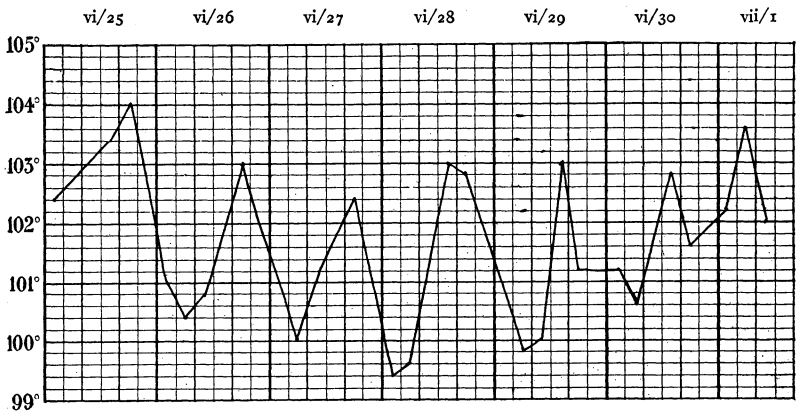
[5] See also the report by Vagedes, *Klinisches Jahrbuch*, 1905, 6, p. 517.

but in neither had it showed any such properties. During this illness she had lost 25 pounds in weight.

Examination at the time of admission into the hospital revealed a few enlarged cervical glands, a coated tongue, some tenderness in the left hypochondriac region, a high pulse, and a variable temperature. The blood seven days after entrance showed 20,500 leucocytes, hemoglobin 60 per cent. The urine contained a trace of albumin and a few cells thought to be leucocytes.

She left the hospital on May 25 and for three weeks tried outdoor living and forced feeding, but became steadily weaker and lost in weight. Her temperature every evening was high, and the latter two weeks of this period she was troubled with frequent and painful urination. Her pulse ranged from 90 to 120. Shortly after she left the hospital a rash appeared on the neck and chest, with bluish or purple blotches on the legs, arms, chest, and abdomen. The bowels were sluggish, and she had epistaxis frequently.

Fig. 1.—Temperature Curve. June 25 to July 1.



When she returned to the hospital she was pale, the conjunctival vessels engorged; there was a bluish-red spot 2 by 4 mm. in the conjunctiva near the left pupil, and a similar but larger spot on the bulbar conjunctiva of the right eye; the cervical glands were enlarged. There were discrete, closely set, light-brown, slightly elevated spots, 2 to 3 mm. in diameter, on the neck and abdomen; likewise purplish ecchymoses on the extremities, chest, and abdomen. The abdomen was tympanitic and tender in various regions.

Examination of the blood on June 25 showed 3,050 leucocytes, hemoglobin 60 per cent; on June 27, 9,450 leucocytes, 2,800,000 erythrocytes, and hemoglobin 47 per cent. The urine was cloudy, reddish brown in color, neutral in reaction, with a specific gravity of 1025, and no odor; it contained albumin, leucocytes, and erythrocytes. The temperature from June 25 to July 1 is shown in the accompanying curve. She was unable to eat, restless and wakeful, and complained quite frequently of pain in the abdomen and severe pain on urination. The stools were large in amount, brown in color, and of semi-solid consistency. She vomited occasionally and had frequent epistaxis. Rectal food was retained quite well, but occasionally expelled, and on these

occasions was tinged red with blood. She became very weak, and on June 30 was delirious, seemed to be in great pain, and died on July 1.

Anatomical changes.—At the postmortem examination by Dr. Rosenow one hour after death the following changes were found: Hyperplasia of the intestinal lymphoid tissue; hyperplasia of the mesenteric, retroaortic, and iliac lymph glands; acute splenitis; subcutaneous and submucous hemorrhages in the urinary tract; renal and urinary calculi; cloudy swelling of the liver and kidneys; fatty liver; sordes; recent and ancient pelvic peritonitis; hydro- and hemato-salpinx; hemorrhages in the right ovary; horseshoe kidney; accessory spleen; sclerosis of the aorta and coronary.

"The body is 135 cm. in length, the abdomen is rather full, though not distended. Brownish spots are present over the anterior surface; on the right breast they are more purple and measure here from 1 to 4 mm. in diameter. Some of the spots are recent subcutaneous hemorrhages and measure 1 to 4 cm. in diameter. The largest are on the right side mainly, the arm, forearm, breast, hip, and thigh. The lining of the mouth shows no changes."

Deserving of special attention are the changes found in the intestinal glands and the urinary tract.

"The lymphoid tissues in the small intestine are slightly enlarged, the solitary follicles not exceeding 1.5 mm. in diameter. Very slight erosions of their surfaces and of the surfaces of the Peyer's patches can be seen on close scrutiny. By holding the small intestine to the light the Peyer's patches appear to contain more blood than the adjacent wall. The large intestine shows no changes. The mesenteric and peripancreatic lymph glands are all enlarged, some measuring 3.5 cm. in their longest diameters, firm and light gray on the cut surface. In the iliac and periaortic glands, also markedly enlarged, hemorrhages are present, and these glands are softer."

Some glands about the aorta were so full of blood that they were thought to be hemolymph glands by Dr. Rosenow.

"The spleen, which is soft and has all the characteristics of an acute infectious disease, weighs 260 grams. On the surface exposed by sectioning the Malpighian bodies are not especially distinct. A small accessory spleen shows a similar appearance.

"In the kidney, which is 'horseshoe-shaped,' there are extensive hemorrhages in the mucous lining of the pelvis. On the cut surface the kidney is mottled with gray and grayish-red areas; the cortex appears swollen. In the upper part of the pelvis are some soft, small calculous masses. Similar submucous hemorrhages are much more marked in the bladder, which also contains soft, small calcareous masses similar to those in the kidney. The hemorrhages are so excessive that but little of the more normal pale mucosa is visible.

"In the right ovary the contents of two cysts, together the size of a hen's egg, appear to be almost pure blood; there is no clot, and the linings are smooth. The outer end of each Fallopian tube is closed by the fibrous adhesions, which are abundant in the small pelvis. Both are distended, the contents of the right are clear, of the left chocolate-colored."

Bacteriological examination.—A short, actively motile bacillus, decolorized by Gram's method, was obtained from the blood during life, and postmortem from the spleen, pelvic lymph glands, heart's blood, peritoneal fluid, left tube, and from the bile. *Staph. pyogenes aureus* was isolated from the pericardial fluid, but was not present in the other material examined.

On agar plates the superficial colonies of the bacillus appeared as circular spots

of a dull gray color by reflected light and bluish gray by transmitted light. They were smooth and moist, with finely crenated edges. The deep colonies were generally spherical and more opaque than the superficial ones. On potato the bacillus grew well after one or two days, the cultures being smooth, raised, moist, bluish white in color, without odor and discolorations. On blood serum it grew well, the growth being white, raised, moist, causing a white turbidity of the water of condensation. In broth a uniform cloudiness appeared in 24 hours, and gradually a white precipitate settled out which was easily diffused again. On gelatin there was a thin white growth along the line of inoculation, but no liquefaction. In glucose-agar stabs gas was formed in 24 hours which obscured the characteristics of the growth. In litmus milk there was at first a slight acidity, which changed in five days to alkalinity, which gradually became more pronounced and permanent. There was no coagulation at the end of four weeks. Indol tests gave negative results. Neutral-red agar turned yellow near the center in 24 hours, and this yellow color gradually extended to the bottom of the tube, but never to the surface. In nine days the yellow color disappeared, and the medium returned to its red color.

By growth in fermentation tubes the following gas formulae were obtained for the carbohydrates indicated:

Glucose*..... $\frac{8.5}{2.5}$	Amylose .....a trace	Lactose* ..... $\frac{0}{0}$
Maltose*..... $\frac{8.5}{3.5}$	Arabinose .....a trace	Nutrose*..... $\frac{0}{0}$
Galactose*..... $\frac{7.5}{2.5}$	Dextrin .....a trace	Inulin*..... $\frac{0}{0}$
Saccharose*.... $\frac{4}{1}$	Isodulcite .....a trace	Raffinose..... $\frac{0}{0}$
Mannit*..... $\frac{4}{1}$		Mannose ..... $\frac{0}{0}$
Melitose..... $\frac{5}{1}$		
Levulose..... $\frac{5}{1}$		

*Repetition twice showed the same results.

The serum of a rabbit immunized by injections of broth cultures of the Buxton paratyphoid bacillus,[1] seven injections in a month, agglutinated this bacillus in a dilution of 1 to 1,000 in 20 minutes, the organism from the Wells-Scott case in a similar dilution in 30 minutes. Immune serum obtained with the Wells-Scott organism[1] agglutinated this organism in a dilution of 1 to 1,000 in 40 minutes and the Buxton bacillus in 45 minutes. The immune serum of a rabbit injected with the bacillus from this case over a period of two months and at intervals of four to seven days, agglutinated the Buxton bacillus more strongly than the Wells-Scott organism—the former in 1 to 1,000 in 40 minutes; the Wells-Scott organism in a dilution of 1 to 900 in 70 minutes.

All the immune sera naturally agglutinated the organisms inoculated; none of them the typhoid bacillus.

Microscopic anatomy.—The intestinal glands are spread apart by hyperplasia of the lymphoid tissue, and their outer portions have suffered mechanical removal in places. There is no surface necrosis of the glands or interglandular projecting lymphoid tissue. The hyperplasia of the lymphoid tissues is characterized

[1] For cultures of both these organisms we are indebted to Dr. N. McLeod Harris, of the University of Chicago.

by the presence of large cells scattered throughout the mucosa and submucosa in wide zones about the lymph nodes, the proportion of such cells over the small lymphoid cells of the node increasing with the distance away from the center of the node. The lighter-stained germinal centers of the lymph nodes are small, and cell division is not marked. In the outer parts of the nodes the large cells are first met with, and in such places the usual arrangement of the lymphoid cells in rows is absent. The large cells[1] are two to four times the size of the small lymphocytes both in their nuclei and the cytoplasm. They often contain two, three, or even more nuclei, and in shape alone resemble, in some instances, the polymorphonuclear neutrophiles; their much greater size and the fainter stain of the nuclei, however, are conspicuous differences. Their nuclei stain like those of endothelial cells. Phagocytosis by these cells is not marked in the intestine, inclusions of either red cells or lymphocytes being rarely found, but these large cells are frequently in process of dividing. It is difficult to discern any relation between the large cells as regards origin and the endothelium of either blood or lymph channels. They occur in rows between the fibers of the submucous coat where there are no channels, and in such places mitotic division is abundant. Many of the small veins seem to be packed with these cells. Polymorphonuclear leucocytes and plasma cells are very scarce in these intestinal lesions, and the changes described are found only in connection with the lymphoid tissues of the bowel, the intervening intestine showing no changes. From this description it is evident that the process in the bowel differs from the changes peculiar to typhoid fever as described by Mallory[2] in certain details—its lesser severity, the limitation to the outer zones of the lymph nodes, the relatively little phagocytosis, and absence of ulceration.

In the capillaries of the liver these large cells are very numerous, and in a few small places, scarcely larger than the field of the immersion lens, the liver cells are absent, and these cells are aggregated with a few polymorphonuclear leucocytes. A few of the large cells contain red cells and masses of hemoglobin, and a few are found with dividing nuclei.

Examination of the lymph glands reveals the wide sinuses filled mainly with the large cells, giving an appearance not unlike some forms of tumor metastases, especially the secondary growths in the inguinal glands from the so-called sarcomas of the testicle. The appearance is also somewhat similar to the large-celled hyperplasia of tuberculous lymphadenitis. The cortical nodules and germinal centers are small, and the large cells, as in the intestine, are first met with in the outer zones of the nodules. Inclusions of red cells are more numerous than in the bowel or liver, and phagocytosis of other cells is difficult to find. Dividing nuclei in these cells are very abundant, 12 to 20 in a single immersion-lens field being readily found. In some of the glands hemorrhages have taken place, and in many the sinuses contain a great deal of blood. Partial and total occlusion of sinuses by thrombi occur in some glands; plasma cells are scarce. In the adipose tissue of the mesentery there are large districts filled with these large cells, and dividing nuclei are very numerous among them. Numerous large lymph channels also occur filled with the large cells.

The changes in the spleen are the presence of many of the large cells in the sinuses, with included red cells and dividing nuclei. Masses of hemoglobin, made up apparently of agglutinated red cells, also occur in the sinuses. Serial sections in paraf-

[1] Throughout the description these cells are referred to as "large cells," and a discussion of their nature is taken up later.

[2] *Jour. Exp. Med.*, 1898, 3, p. 611.

fin of entire Malpighian bodies show no changes in these structures. The plasma-cell content of the spleen is not excessive; many are aggregated about masses of blood pigment.

In the adrenal there are foci of necrosis similar in all respects to those in the liver, except that they are more minute. The large cells in the capillaries are found free, with dividing nuclei and inclusions of red cells or hemoglobin masses, occasionally with included mononuclear leucocytes, but the capillaries do not contain the great number of these cells seen in the corresponding channels in the liver. Small aggregations of two to four or six plasma cells and mononuclear leucocytes occur in the capillaries.

In the tunica propria of the esophagus the changes are interesting because limited to a hyperplasia of large cells. The process is easily traced to the perivascular tissues where lymph channels course and have their origin. Just without the most minute arterioles close to the epithelium and in the dense fibrous tissue these cells occur in small groups and short rows. Evidences of their multiplication, mitotic figures, are not numerous in such places, but a little deeper in the wall where the vessels have slightly larger calibers there are found large swollen channels filled with these cells. These channels have walls like veins, but the absence of blood and their content of large cells speak for lymph channels. Between these two places in the esophageal wall, the most minute perivascular groups of these cells, and the large channels filled with them, there are collections without the blood vessels of such cells with numerous dividing nuclei as numerous certainly as in many of the more slowly growing carcinomas. The lymph nodes in the tunica propria of the esophagus where these changes are found are small, normal, and quiescent. There are no signs of phagocytic processes in the esophagus.

In sections of the tongue changes similar to those in the esophagus occur, but the process is not as marked, mitoses not as numerous. Deep in the musculature of the tongue arterioles occur in which most of the cells are the large cells. Other vessels have apparently a normal blood content.

The stomach shows no important changes. The lymph nodes in the mucosa show no signs of cell production; plasma cells are abundant between the glands.

In sections of the lung excellent opportunity is found for study of the finer details of the large cells. Their most striking feature has already been mentioned—a similarity to the polymorphonuclear neutrophiles in the shape of the nuclei. Many have two nuclei, the nuclei are rarely round when single, and often two large hemispherical nuclei lie together by the flat sides; in many the nuclei are apparently clusters of small nuclei. When the nuclei are large there is but little cytoplasm. An excentric position of the nucleus occurs in some cells, but is not common. No granules occur in the cytoplasm. The gigantic nuclei in some of these cells remind one forcibly of certain marrow cells, and especially when the nuclear material is so aggregated that clear portions remain in the center. In some of these cells there are inclusions of either polymorphonuclears or lymphocytes, but inclusions generally, and of red cells in particular, are not numerous. The dense appearance of the chromatin in some cells and their odd shape suggest the results of fixation upon dividing nuclei; in others the chromosomes are quite definite and the phases of mitosis easily recognized. Most of the small arterioles contain these cells abundantly, in those with walls two to four times the width of the endothelial nucleus the content is almost entirely of these large

cells. In the capillary network they are so numerous that the resemblance to leukemia is again striking (see Fig. 2).

In the vessels of the pancreas, especially the capillary network, it is difficult to find the large cells; in the myocardium and thyroid they are present, but not abundantly.

The changes in the kidney are remarkable. In sections stained with hematoxylin and eosin there are seen, with the unaided eye, sharply demarkated, dark, oblong areas in the cortex, the largest 5 mm. in length (see Pl. 4, Fig. 1). As a rule, these are wider near the cortex, but some have a fairly uniform width of 1 mm. or less. Some smaller dark spots occur just beneath the capsule unconnected with the deeper oblong areas, and they are flattened out against the capsule, their long axes parallel to it. In addition to these are smaller dark patches in the cortex, but almost invariably slightly oblong and, like the first mentioned, with their long axes at right angles to the capsule. In the base of the medullary pyramid also are dark patches, but not as dark as those in the cortex and with very vague outlines. With a hand lens or the low power of the microscope these patches are found quite uniformly limited to the medullary rays, except where in the outer parts of the cortex, widening out, they include the labyrinth intervening between the rays. With higher powers these appearances are found to be due to the aggregation in these places of cells mainly of the type described as prevalent in the lymphoid tissues and uterus. At the margin of the infiltrated region the capillaries are dilated and filled with these large cells—a condition that becomes more marked as the regions are entered. It is only by prolonged search that the large cells are found in process of migration through the capillary walls; migration of the small lymphocytes, although not at all a marked feature, is more readily found. The process by which the large cells have reached the outside of the vessels seems to be for the most part through rupture of the distended capillaries. About and within the margins of these cell aggregations there are, between the capillaries and basement membranes of the tubules and parallel to them, long rows of large cells. In the capillaries adjacent to such rows there are also many of the large cells, by actual count as many as, or even more than, of red cells; yet practically none of the large cells are in process of migration through the wall. The cells in the rows between

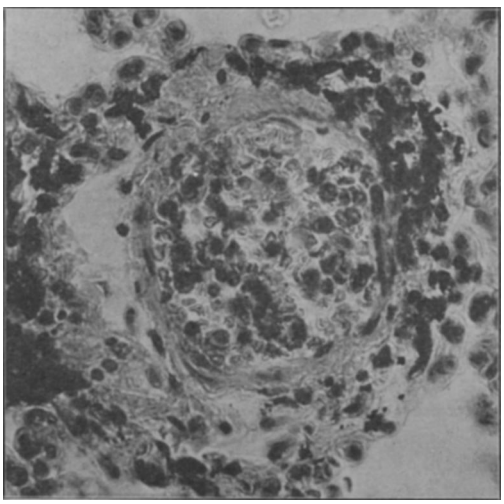


FIG 2.—Showing the great number of large cells—large mononuclear leucocytes—in an arteriole in the lung and the resemblance to the appearances met with in leukemia. The vessel is surrounded for the most part by a deposit of coal pigment. (× 375)

capillaries and tubules have evidently attained their location by infiltration outward from the denser portions. The explanation for the accumulation of these large cells in such remarkable numbers by a dilatation and rupture of the capillaries is not in accord with the absence of hemorrhage as a conspicuous feature of the focal lesions. Some free red cells occur within the field of infiltration, but they are not numerous. That greater hemorrhage has not taken place may be accounted for by the blocking of the capillaries with the large cells and by compression of the vessels within the regions; for the large cells without the capillaries have multiplied extensively. The increase through karyokinetic division of the large cells is an important feature explaining the cell masses. In practically any field of the oil immersion lens six or eight dividing nuclei may be found in these areas, and they are almost invariably in cells without the vessels. We have been unable to find dividing nuclei in the endothelium.

The glomeruli are not seriously altered except where they have been included in the aggregations of cells or otherwise secondarily affected. Where the cells are most densely collected the renal parenchyma is absent. Some tubules contain hyalin casts, and in the epithelium of some, especially the collecting tubes of the pyramid, there are round, brown granules. Good fixation was attained, the brush markings of convoluted tubule epithelium being quite generally present. In the base of the medullary pyramids the infiltration with these cells is more uniform, not so dense as in the cortex, and this explains the absence of sharp demarkation for the dark regions seen in such places when examined with the unaided eye. Deeper in the pyramid, however, there are focal lesions, but small, and it is in these minute collections that the method of origin of the lesions is most readily traced to a blocking of the capillaries. These small foci are located always where the parallel vessels, brushlike in their arrangement, are found; they are rarely wider than the width of two or three of the adjacent collecting tubules. In the pelvic mucosa there are aggregations of these large cells and more of the small mononuclear leucocytes than are found in the more proximal lesions, and in such exudates hemorrhage has occurred. Short, thick bacilli, corresponding in size and shape with typhoid bacilli and destaining by Gram's method, are found in the blood vessels, and aggregations of cells in the cortex; in the pryamids they occur in the collecting tubules where there is no evidence of inflammatory processes. They also occur in the blood vessels of the pyramid in the small cell aggregations described, and are numerous in the lesions of the pelvic mucosa. It is impossible to find the bacilli within cells, the large cells especially being examined with that in mind.

The changes in the uterus are entirely in the musculature. At first glance, with the low powers, one is reminded of leukemia, but a moment's inspection determines that the collections of cells are without the blood vessels and in lymph channels. Just beneath the endothelium of the large venous sinuses the cells are met with, and in all respects the appearances are quite similar to the changes in the esophagus. The cells are the same large cells, and a short distance from the endothelium of the large veins the lymph channels are found distended with them; mitotic nuclei are abundant (see Pl. 4, Fig. 2). There is considerable loose fibrous tissue about these large veins, and where the section has been across the veins and their channels are somewhat stellate, from the edge of the projecting rounded fold, marking the lining of the vessel to the musculature, the loose tissue is the seat of a very active production of these cells. There are no lymph nodes, but shortly beneath the vein lining the cells become arranged in rows which terminate in channels with thin walls and no content of red

cells. The lymph channels course parallel with the blood vessels. This change is more marked toward the lining of the uterus than toward the serosa, and in many places in the musculature there are rows of the large cells where lymph channels are not evident nor blood vessels of dimensions larger than capillaries.

The changes in the musculature of the bladder are similar to those in the uterus, but not so marked. Hemorrhages are not limited to the mucous and submucous coats, but are present in the musculature. In places the lining of the bladder is absent. The alterations of the inner coat resemble those in the renal pelvis.

The production of the large cells in the ovary is marked; mitoses are abundant. The lymph channels are not so readily traced as in the uterus; the cells are less commonly in rows. Large regions occur in which these cells are so abundant that with the higher powers the field is quite like the lymph glands.

The cultural reactions of the bacillus isolated entitle it to a place in the group of organisms intermediate between the colon and typhoid bacilli; the transient acidity and terminal alkalinity in litmus milk and neutral red agar refer it to the secondary group which includes the "paratyphoid B" of Schottmüller, de Feyfer and Kayser, *Bacillus enteritidis*, and the organism of hog cholera.[1] Some doubt may remain as to which of these it is most closely related,[2] since interagglutination experiments were carried out with immune serum produced by known strains of paratyphoid organisms, and not with the other members of the intermediate group such as *B. cholerae suis* and *B. enteritidis*. Its widespread occurrence in the body shown by the cultures made at the postmortem examination, its recovery from the blood during life, and the presence of bacilli in the tissues, all indicate its etiologic significance. Bacteria of the hog cholera group may cause sudden acute disease such as occurs in food poisoning, but their etiologic rôle in prolonged illness with some of the features of typhoid does not seem so probable. The relatively high agglutinative powers of the immune serum for known strains of paratyphoid bacilli[3] also to some degree indicate a lack of close affinity with *B. enteritidis*.

Material from the bone marrow was not obtained at the postmortem examination, nor any blood at that time for subsequent agglutination experiments; the reports of failures of the blood serum to agglutinate typhoid bacilli, during the life of the patient, are quite trustworthy; it is quite difficult to account for the changes in the

[1] Boycott, *loc. cit.*

[2] Trautmann (*Zeitschr. f. Hyg.*, 1903, 45, p. 139) prefers to call them all paratyphoid organisms.

[3] See the tables of interagglutination by Boycott.

kidneys by an ascending infection of the urinary tract; a remarkable discrepancy exists between the leucocyte counts made during life and the great numbers of nucleated cells found in the vessels of many of the organs. All of these facts in one way or another affect the relations of the conditions in this case to existing classifications of disease-processes, for this interesting array is presented: symptoms leading to suspicions of typhoid fever; later a purpura hemorrhagica clinically; an anatomic diagnosis of acute interstitial nephritis and typhoid fever, the latter tentative, at the postmortem examination; bacteriologically a generalized infection with a paratyphoid organism; and histologically many of the features of an acute lymphatic leukemia.

In the pathological anatomy of paratyphoid fever as depicted by Wells and Scott,[1] the absence of lesions in Peyer's patches and the solitary follicles is emphasized. In the case since reported by Ascoli,[2] however, an enormous number of freshly formed cicatrices—death on the thirty-third day of the disease—were found in these structures.[3] In both Ascoli's case and the one reported here the mesenteric glands were markedly swollen, a feature only recorded in one of the five cases collected by Wells and Scott. Other exceptions in our case are the proliferative changes in the intestines, the occurrence of the large ("endothelial") cells in the focal necroses in the liver, and no remarkable splenic enlargement. It is difficult to exclude Ascoli's case as one of genuine paratyphoid fever, since the repeated tests of the serum during life were made with a typhoid bacillus of high agglutinability toward known typhoid immune serum, while the bacillus recovered from the spleen during life, and from the spleen and blood postmortem, corresponded in its cultural reactions to the paratyphoid bacillus, variety "B," although its ability to ferment a number of carbohydrates is not recorded.

In the report by Tuttle[4] of an epidemic of paratyphoid fever affecting seven persons, there are many circumstances similar to the conditions related in accounts of food infections, but the opinions expressed in the discussion were in favor of its origin in the drinking-water obtained from a tank. Nothing was discovered, however, when the tank water was examined. The description of the lesions

[1] *Loc. cit.* [2] *Loc. cit.*

[3] Swollen Peyer's patches were the only lesions found in the one fatal case of food poisoning (seven persons) due to the paratyphoid bacillus "B" reported by Vagedes (*loc. cit.*).

[4] *Proc. N. Y. Path. Soc.*, 1903, 3, n. s., p. 185.

found in the postmortem examination of the one fatal case, although not very detailed, confirm the statements of Wells and Scott as to the pathological anatomy. The spleen was not markedly enlarged, 6¾ oz., but the intestinal lesions were limited to the lower two inches of the ileum, where there were four or five small ulcers. Both large and small bowel contained large amounts of blood.

The purpuric hemorrhages in this case are quite similar to those observed by Sacquépée[1] in eight soldiers of the garrison in Rennes who within a short time of one another became acutely ill; his account is in many respects like those of food poisonings, but the source of the infection was not determined. In some the skin lesions were roseolae; in others, dark-red patches, disappearing after 8 to 12 days, leaving small, brown-pigmented areas. The serum—1 to 500 to 1 to 2,000—of these patients agglutinated the "B" form of the paratyphoid bacillus, and that organism was recovered from the blood with a coccus (enterococcus Thiercelin) in four cases; in the other four the coccus alone was obtained. Intestinal hemorrhages were a clinical feature of the case reported by Wells and Scott.

There are a number of reasons for excluding an ascending infection of the urinary tract in this case: the active production of the large cells in the lymph glands and intestinal lymphoid tissue, and the evidence afforded by the uterus, bladder, and ovary that in all likelihood the process was even more widespread than demonstrated; the evidence that these cells were carried to the kidney in the blood current; and finally the character of the process in the kidney. The usual ascending infections of the kidney cause an inflammatory process characterized by a peculiar sequestrating necrosis, and the changes are very marked in the collecting tubules of the medullary pyramids. Not only were such changes absent in the kidney of this case, but it is doubtful if the process of infiltration with the large cells and their subsequent multiplication can with propriety be considered as an inflammation. The process in the kidneys in scarlatina and diphtheria designated by Councilman[2] as nephritis (acute interstitial) in one respect at least resembles an inflammatory process more than the lesions in this case; he found that the lymphocytes and their derivatives, the plasma cells, migrated through the vessels; migra-

[1] *Arch. de méd. expér. et d'anat. path.*, 1905, 17, pp. 718–28.

[2] *Jour. Exp. Med.*, 1898, 3, p. 393.

tion of the large cells in this case through the vessels is so inconspicuous and difficult of demonstration that it does not account for the focal collections. Then, too, the large cells do not correspond to the leucocytes (polymorphonuclear, eosinophilous, and small lymphocytes) which, with red cells, constitute to such a large extent the adventitious cells of both acute and chronic inflammations. With the exception of an absence in this case of extraglomerular collections of the large cells, the focal lesions are quite similar in their distribution to those described by Councilman in acute interstitial nephritis, subcapsular, about the pyramidal veins, in the boundary zone and the medullary rays of the cortex. The macroscopic appearance of the kidney also is that of acute interstitial nephritis and totally unlike acute ascending inflammations.

As to the character of the large cells, they resemble mostly the large lymphocytes, and in this conclusion Dr. Joseph A. Capps agrees with us, although he suggested a similarity between some of them and myelocytes. In many respects they correspond to the cells Mallory[1] refers to as "endothelial cells," in their occasional inclusions, the curved, indented nuclei, and marked proliferative capacity. Indubitable origin from pre-existing endothelial cells was not demonstrated for these large cells, although it is probable that the lining cells of lymph channels, at least of the very minute, contributed to their production. In conclusion, the similarity with lymphatic leukemia of the histologic changes and the absence of any notable increase of leucocytes in the circulating blood seem irreconcilable; a similar idea impressed Councilman in his study of acute interstitial nephritis. The necessity of a broader conception of inflammation to include such processes of hyperplasia, metastasis, and proliferation in the secondary deposits has been emphasized by Mallory,[2] and is well illustrated by this case.

EXPLANATION OF PLATE 4.

Fig. 1.—Illustrating the shape and limitation to the cortex of the accumulations of cells. A slight darkening of the boundary zone is shown, as well as minute foci in the medullary pyramid. (× 7½)

Fig. 2.—The perivascular formation of the large cells in the uterus. The obliquely directed opening is a vein; to the left is a small artery and a lymph channel, black and densely packed with the large cells. In the loose tissue between these structures and the musculature the large cells are numerous and karyokinetic nuclei in them very abundant. (× 175)

[1] *Jour. Exp. Med.*, 1898, 3, p. 611. [2] *Ibid.*, 1900–01, 5, p. 1.

PLATE 4.

FIG. 1.

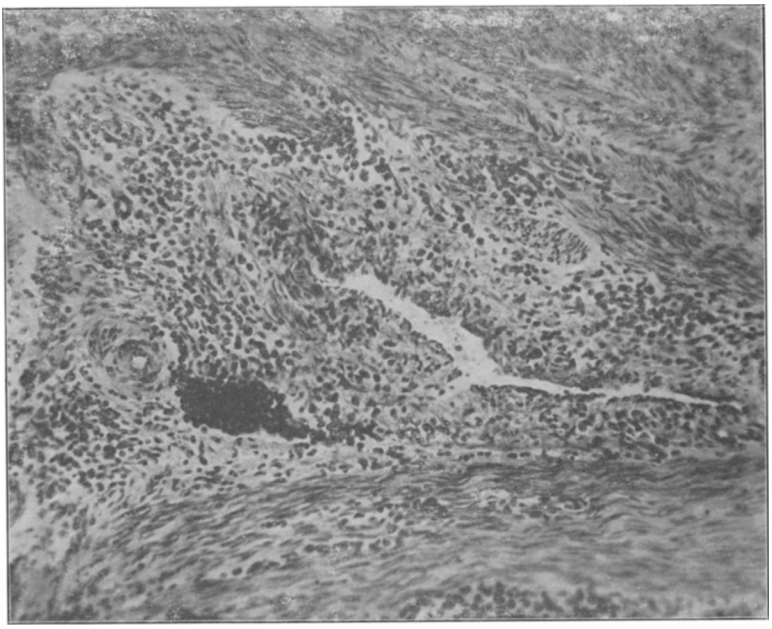


FIG. 2.